Clinical Evaluation of Patients with TMJ Implants

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Abstract

An undetermined number of patients with temporomandibular joint (TMJ) symptoms have been treated with intra-articular disc implants composed of Teflon ethylene/propylene or Teflon polytetrafluoroethylene and aluminum oxide (Proplast-Teflon). These implants have demonstrated the potential to fragment *in situ* resulting in non-biodegradable particles that stimulate a giant cell reaction leading to pain and degeneration of local structures. Subsequently, many of these patients report severe pain and limitation of mandibular opening and nonspecific systemic complaints. This case series (N=32 patients) examined the possible relationship between TMJ implants and persistent pain, responses to sensory stimuli, quality of life, and immune dysfunction. Laboratory and clinical assessments included orofacial pain symptoms, neurologic function, clinical signs and symptoms of rheumatologic disease, physical function, and behavioral measures. We found that TMJ implant patients appeared to have altered sensitivity to sensory stimuli, a higher number of tender points with a diagnosis of fibromyalgia, increased self-report of chemical sensitivity, higher psychological distress and significantly lower functional ability. Systemic illness or autoimmune disease was not evident in this series of TMJ implant patients.

Key Words

Chronic pain, orofacial pain, TMD, TMJ implant, fibromyalgia

Introduction

Various non-surgical strategies have been advocated for the treatment of patients with temporomandibular disorders (TMD) including medications,[1,2] splints,[3,4] physical therapy,[5,6] and trigger point injections[7] to relieve pain, reduce inflammation, improve temporomandibular joint (TMJ) function, and prevent structural damage or disease progression. Patients who are not responsive to these treatments may be offered surgical treatment ranging from TMJ arthroscopy, TMJ lavage, disk repair, or joint replacement (for review see Mercuri[8]). Silicone rubber and Proplast/Teflon implants were the most commonly used devices in TMJ reconstructive surgery in the 1980's. Silicone rubber was first introduced in 1968 as a TMJ implant material for temporomandibular joint reconstruction[9] followed in 1970 by Proplast/Teflon (Vitek) with a similar indication.[10-13]

Despite the short-term clinical success initially reported for these alloplastic implants, they were found to degrade in most patients when subjected to biomechanical joint forces, resulting in localized granulomatous reactions at the joint area, degenerative changes, persistent joint pain, and joint dysfunction.[14-20] The extent of problems associated with TMJ alloplastic implants and the characteristics of patients who have unsuccessful outcomes with these implants remains unclear in the absence of controlled epidemiological studies. However, clinical reports indicate that some TMJ implant patients developed chronic orofacial pain, impaired jaw function, and further structural changes (for review see Wolford,[21] Fontenot,[22] and Milam[23]). Furthermore, there have been concerns by patients and clinicians about the potential incidence of connective tissue and autoimmune diseases that might be attributed to the implant material.

This case series was designed to describe the clinical, laboratory, psychological and systemic immunologic characteristics of patients with TMJ Proplast implants and to examine the possible relationships between patients with these implants and their pain, responses to sensory stimuli, quality of life, and autoimmunity.

Methods

Study Subjects

Patients with diverse clinical presentations were recruited for this cross-sectional, observational study. They were referred from regional university-based orofacial pain centers and private practices from across the United States. Eligible for study were patients who had history of TMJ implant placement, complete medical and dental records, and written referrals from their primary clinician. Prior to entering the study, records were reviewed and phone interviews conducted for all patients. Thirty-three patients met screening criteria and were invited to participate. One patient presented with cardiovascular instability at NIH admission and was discharged to her primary physician after her condition stabilized, resulting in N=32 patients who were evaluated. Patients underwent an interdisciplinary assessment as outpatients in the NIH Clinical Center as participants in a protocol approved by the National Institute of Dental and Craniofacial Research's Institutional Review Board. Patients were examined by specialists in orofacial pain, neurology, rheumatology, physical medicine and rehabilitation, and psychiatry. History and previous medical information, including the results of past laboratory investigations, medical consultations, and radiographs were also reviewed.

The possible development of sensitization was examined by systematic evaluation for the presence of specific tender points using generally-accepted criteria for diagnosing

fibromyalgia, and by measuring responsiveness to thermal pain stimuli. To evaluate the impact of chronic pain on quality of life, self-report questionnaires for psychological and health outcome measures were administered. Patients were examined for the presence or absence of features consistent with environmental sensitivity. Rheumatological assessment was performed for the presence of autoimmune disease and inflammatory rheumatic disorders including autoimmune serology. Blood samples from consecutive patients were evaluated with investigational assays to investigate whether there was evidence of systemic alterations in immune measures that might not be detected by clinical evaluation and routine clinical laboratory tests.

Clinical Exams

An orofacial pain evaluation was performed by a dentist trained in orofacial pain. This evaluation consisted of medical/dental history review, a head and neck examination, assessment of joint function, palpation of the masticatory muscles and the TMJ, and an intraoral dental examination. TMD diagnosis was classified using axis I of the Research Diagnostic Criteria (RDC) for temporomandibular disorders.[24] A complete rheumatological examination was performed by a rheumatologist for the presence of musculoskeletal or autoimmune disorders, including fibromyalgia, using the American College of Rheumatology (ACR) classification criteria.[25] The ACR criteria for fibromyalgia include widespread somatic pain and the presence of ≥ 11 of 18 specific tender points as diagnostic features of this disease. Tender points are defined as areas of hyperalgesia/allodynia where localized pressure of ≤ 4 kg per 1.54 cm^2 with a dolorimeter (Pain Diagnostic and Thermography, Great Neck, NY) elicits pain. Neurological evaluation was performed by a neurologist for motor, sensory and cranial nerve assessment to rule out nerve injury, complex regional pain syndrome, and other neurological disorders. Vertebral alignment,

posture evaluation and testing of cervical, shoulder, and extremity muscles, along with cervical and TMJ range of motion, were assessed by a physical medicine and rehabilitation consultant. Psychiatric evaluation was performed by a psychiatrist in accordance with the DSM-IV.[26]

Laboratory Tests

Blood samples were collected between 8:00 AM and 9:00 AM on each patient's first visit day. Standard diagnostic tests were conducted by the NIH Clinical Pathology Laboratory for blood chemistry, hematology, liver, kidney and thyroid function, rheumatic and connective tissue disease indicators, and infection. Viral tests included screening for HIV, hepatitis B and C, and syphillis. Tests of immune status consisted of anti-nuclear antibody (ANA), anti-DNA, anti-neutrophil cytoplasmic antigen antibodies (ANCA), anti-Smith antibodies, C-reactive protein, rheumatoid factor, immunoglobulin (IgA, IgG, IgM), and complement C3/C4.

Immunological Studies

Mononuclear leukocytes were isolated by density gradient (Ficoll-Hypaque) centrifugation of heparinized peripheral blood from TMJ implant patients and healthy volunteer controls as described in a previous study.[27] Mononuclear cells were stained with antibodies to cell surface antigens to define leukocyte subsets and analyzed by fluorescence activated cell sorter (FACS).[28] Additional mononuclear cells ($2x10^5$) were cultured for mitogenic and antigenic stimulation as described previously.[27] Results are presented as a ratio of tritiated thymidine uptake into DNA of stimulated cultures to unstimulated cultures (stimulation index).

Clinical Pain Assessment and Measurement

Subjects were asked to rate their usual level of orofacial pain during the month preceding their visit as well as their present orofacial pain. Separate visual analogue scales

(VAS) for pain intensity and pain unpleasantness were used. [29] The VAS consisted of a 100 mm line, anchored with the extremes of pain intensity represented as "no pain" and "worst pain possible" and the extremes of pain unpleasantness represented as "not bad at all" and "the most unpleasant feeling possible".

Experimental Pain Assessment and Measurement

Twenty-three of the TMJ implant subjects were compared to twenty-three age and gender matched pain-free volunteers selected systematically from a pool of 240 participants in a concurrent study. VAS for sensory intensity and affective components of pain were used to rate heat stimuli (43° to 49°C) of 5 sec duration administered in a random order and delivered to the ventral forearm of subjects by a hand-held contact thermode. Stimuli were applied in an intermittent manner to avoid the possibility of habituation, sensitization, or suppression of cutaneous receptors.[30,31]

Environmental Exposure Measures

The Quick Environmental Exposure and Sensitivity Inventory (QUEESI) is designed to evaluate patients for the presence of symptoms that might be attributed to chemical exposures such as disseminated implant particles. The QUEESI is a self-administered 50-item questionnaire that contains four core scales: Symptom Severity, Chemical (Inhalant) Intolerance, Other Intolerance, and Life Impact. The four core scales of QUEESI have been shown to be reliable, valid, and correlated with standard survey measures of health status and life functions.[32] To identify subjects likely to be chemically sensitive, the scores from each of the four core scales were tallied to obtain a total scale score (range 0-100). Subjects with scores above the high criteria are considered chemically sensitive based on published normative data.[32]

Psychological and Quality of Life Measures

Three self-report tools were used to evaluate each subject's current level of cognitive functioning, emotional, and psychological status: the Minnesota Multiphasic Personality Inventory (MMPI),[33] Millon Multiaxial Inventory-II (MCMI-II)[34] ; and the Symptoms Checklist-90 (SCL-90).[33] A clinical psychologist blinded to the subjects' medical history and diagnosis scored and evaluated these instruments. In addition, to assess the chronic orofacial pain impact on daily life functioning, usual daily activities, and general well-being, the Rand Health Status Measure (SF-36)[35] and Sleep Quality Index (SQI) were used. SQI is a six-item sleep survey that ranges from 0 to 18, with lower scores representing better sleep.[36]

Statistical Analyses

The data were analyzed using SPSS and BMDP standard statistical packages (SPSS Statistical Software, Chicago, IL). Descriptive statistics are reported as mean ± one standard deviation. All tests were considered statistically significant at $\alpha = 0.05$ without adjustment. The significance of between-group differences for continuous dependent variables was determined by student t-test or one-way analysis of variance (ANOVA) with Tukey's range test used for post hoc testing. For the investigational assays, average marker counts for TMJ implant subjects with fibromyalgia and those without fibromyalgia were compared. All comparisons were separately performed, summarized by 95% confidence intervals on the differences in mean scores, together with the associated p-values for the respective t-test. The same analyses were performed before and after excluding four patients with concurrent Staphylococcus infections at the implant site,

prepatellar bursitis of the knee, and systemic lupus erythematosus (SLE) to avoid bias from the effects of known infections.

Results

Characteristics of Patients with TMJ Implant Surgery

The characteristics of the TMJ implant patients are presented in Table 1. A wide range of symptoms were documented prior to the TMJ surgical interventions; most common were joint noise and pain complaints in the jaw, face, and ear regions. One patient reported a history of trauma from a car accident that resulted in generalized that included the head, neck, and jaw regions. Treatment by nonsurgical modalities prior to TMJ surgery included medications, occlusal splints, orthodontic treatment, physical therapy, and chiropractic treatment. Time to surgical treatment varied from one to six months after the onset of symptoms. All TMJ implant surgeries had been performed using a preauricular approach. Thirty patients had a history of various medical conditions including asthma, epilepsy, hypertension, hypothyroidism, mitral valve regurgitation, migraine headaches, pre-menstrual syndrome, and hernia.

Sensory Sensitivity of TMJ Implant Patients

When patients presented for study evaluation, the majority were still reporting pain and mandibular dysfunction as their chief complaint (Table 1). TMD diagnoses varied among five RDC diagnostic subtypes which are not mutually exclusive (Table 2). Based on VAS ratings of current orofacial pain intensity, the sample was divided *post-hoc* into three subgroups of approximately equal numbers of subjects: minimal pain (score ≤ 42, n=12); moderate pain (score >42 - <80, n=10); or severe pain (score ≥ 80, n=10). The relationship between *post-hoc* classification by self-reported level of present orofacial pain and other factors was examined by

chi-square analysis. A significant relationship was detected between the number of surgeries and present pain intensity ($P < 0.001$), i.e., patients who reported moderate or severe pain at the time of evaluation had a history of more surgeries (Figure 1A). Mandibular range of motion (ROM) was measured as both passive and active maximum opening with and without pain (Table 2). Very few patients presented in the limited range of <10-16 mm. For the palpation examination, the distributions were mixed for all patients across the four pain category ratings with more patients reporting the extremes of no pain or severe pain (Table 2).

We found that TMJ implant patients had evidence of widespread pain and tender points. Close to half of the patients in the moderate (40%) and most of patients in the severe pain group (80%) met ACR criteria for fibromyalgia (Table 3). There was a strong association with the current pain intensity level and the incidence of fibromyalgia diagnosis (Figure 1B). No patients were diagnosed with complex regional pain syndrome, although eight patients exhibited mild sensory impairment including allodynia, dysesthesia, and paresthesia over either the pre-auricular, lip, or facial area.

Clinical and Experimental Pain Assessment.

All subjects rated pain intensity and unpleasantness during thermal pain testing similarly with a significant positive relationship (Pearson's correlation $r= 0.98$, $p<0.01$). There was a significant difference overall in experimental pain ratings between the healthy volunteers and TMJ implant patients ($p<0.01$); TMJ implant patients rated thermal stimuli significantly less painful over the temperature range tested ($p<0.02$) than did healthy volunteers (Figure 2A&B). No relationship was observed between patient response to experimental pain stimuli and clinical pain report.

Quick Environmental Exposure and Sensitivity Inventory (QUEESI).

Patients' scores were compared to population means as well as between the three *post hoc* pain intensity classifications. Compared to the minimum pain group, more subjects in the moderate and the severe pain groups had abnormal QUEESI scores in the four scales of symptom severity, chemical intolerance, other intolerances, and impact on life (Table 4). More than half the subjects in the moderate pain category and three quarters in the severe pain groups scored above the normal range in symptom severity and life impact scales.

Psychological and Quality of Life Measures.

Almost all patients (90%) in the moderate and severe pain groups had mood disorders (primarily depression) as measured by self-report (Table 3). A lower incidence of these diagnoses were made by the psychiatric interviews, but this discrepancy may be due in part to differences in the number of subjects who completed the testing (N=29) and had a psychiatric interview (N=18). Compared to published normative data from the U.S. population,[35] more patients in the moderate and severe pain groups had low quality of life scores across the eight health domains (physical functioning, social functioning, role of physical, role of emotional, bodily pain, mental health, vitality, and general health (Table 5). For the domain of physical functioning and limitations in physical role, all patients in the severe pain group scored below the normal population. In the sleep survey, patients with minimal pain had better sleep scores (3.8 ± 2.02) than subjects exhibiting moderate (9.6 ± 3.2) and severe (9.8 ± 3.9) clinical pain ($P < 0.05$).

Autoimmunity of TMJ Implant Patients

No evidence of rheumatoid arthritis, Sjögren's syndrome, or other autoimmune diseases were found on clinical exam, although one patient had clinical features consistent with possible systemic lupus erythematosis antedating her TMJ implant surgery. This patient had bilateral wrist

synovitis, malar rash and a history of oral and nasal ulcers. This patient did not meet the ACR classifications criteria for SLE[37] which requires meeting 4 of 11 criteria.

Laboratory Findings

There were no consistent abnormalities in chemistry or other blood tests (data not shown). Erythrocyte sedimentation rates were normal. Antinuclear antibodies and rheumatoid factors were not detected. Two patients had an elevation of C-reactive protein. One had a prior diagnosis of tuberculosis infection, and the other had a history of antrectomy due to gastric ulceration. Of the two patients with slight elevation of IgM, both had diagnoses of fibromyalgia and residual Staphylococcus infection at the TMJ surgical sites. One subject had a history of prepatellar bursitis with swelling of the right knee noted months prior to his study evaluation. At the time of his rheumatological evaluation, a synovial fluid biopsy was obtained, and the result was negative for bacterial or fungal infection.

Immunologic Parameters

Consistent with hematologic laboratory findings, phenotypic analysis of the peripheral blood mononuclear cell populations of the TMJ implant patients revealed no consistent alterations in total T lymphocytes (CD3) or in CD4 or CD8 lymphocyte subsets (Fig. 3A). B lymphocytes (CD20), natural killer (NK) cells (CD56), and monocytes (CD14) were comparable among TMJ implant patients and control groups, as were nearly 30 additional cell surface antigens evaluated as markers of potential immune activation (data not shown). Functionally, isolated mononuclear leukocytes proliferated in response to nonspecific mitogens, including PHA and Con A and to specific antigens, such as PPD at levels not significantly different from controls ($p=0.066$, Fig. 3B). However, a decrease in total CD3 positive T lymphocytes was noted, particularly in the severe pain group

(p=0.018, Fig. 3C). CD3 T lymphocytes include both the CD4 helper T cells and the CD8 cytotoxic/suppressor T cells, and while there was no significant difference in percentage of CD4 cells, there was a modest non-significant reduction in the CD8 population (p=0.08) in patients with severe pain. Furthermore, when stratified by fibromyalgia diagnosis, patient differences in lymphoid cell phenotype and function could be detected. Similar to the pain classification, a significant decrease in the total T lymphocyte population (CD3 positive; p=0.02) reflected lesser numbers of CD8 positive cytotoxic/suppressor T cells (p=0.02) in the fibromyalgia patients (Fig. 3D), consistent with the overlap between these two patients populations (Fig. 2). Although proliferation responses to nonspecific mitogens were nondiscriminatory, patients with fibromyalgia were more responsive to antigens (PPD shown, Fig. 3B) than TMJ implant patients without a fibromyalgia diagnosis (p=0.026).

Discussion

The TMJ implant patients evaluated in this study who had undergone multiple surgeries reported more severe pain, and the reported pain was not only localized to the overlying surgical areas of the preauricular region, but often diffused to distant regions of the head, neck, upper back and upper extremities. Although a high proportion of patients in the present sample meet the ACR criteria for fibromyalgia, it is unclear if fibromyalgia predated surgery or resulted from the surgical insult and years of persistent pain. For these patients with failed TMJ implants, continued surgical attempts at re-treatment have been largely unsuccessful and resulted in persistent pain.

The pathophysiology mediating chronic orofacial pain remains unclear. It has been hypothesized that chronic orofacial pain may be due to impaired inhibitory systems within

the central nervous system.[44] Descending pain inhibitory or facilitating pathways could likely play an important role in modulating the excitability of dorsal horn neurons receiving converging somatic input. Recent animal studies have demonstrated the dynamic plasticity of the pain modulating pathways in response to persistent tissue injury.[50,51] In this study sample, the high levels of persistent orofacial pain due to the inflammatory reaction to the failed implant particles and the multiple surgeries could have caused central nervous system hyperexcitibility that may be responsible for the persistence of pain long after initial injury.

TMJ implant patients evaluated in this series exhibited a hypersensitivity to sensory stimuli, including evidence of widespread somatic pain with increased tender points, and reported increased sensitivity to environmental stimuli. Interestingly, these patients rated thermal pain lower compared to control subjects during the experimental pain testing. Naliboff and colleagues reported a similar elevation of acute nociceptive threshold in low back pain patients.[39,40] Using a signal detection model to assess the differences between chronic low back pain patients' and control subjects' perception of radiant heat stimuli, they found that pain patients had significantly higher pain threshold than controls. Our results and Naliboff's support an extension of the adaptation theory,[41] which postulates that pain patients evaluate experimental pain within the context of their previous experiences with pain. In contrast to our findings, other studies have shown that fibromyalgia patients have increased sensitivity to thermal pain testing compared to healthy controls.[42,43]

Findings on experimental pain testing in TMD patients have been mixed. Maixner and colleagues found that TMD patients show an enhanced sensitivity to both thermal and

ischemic noxious stimuli compared to pain-free control subjects.[44] Similarly, Malow et al showed that TMD patients with myalgia have a lower finger pressure pain threshold compared to controls.[45] However, Price and Harkins reported that patients with myofascial pain dysfunction and normal pain-free volunteer subjects provided similar VAS response to suprathreshold noxious stimuli applied to either the face or the forearm.[46] Given the limitation of the present case series where normal and control subjects with other pain syndromes were not included, it is difficult to provide an interpretation for these inconsistencies. Differences in patient populations and the test procedures might have contributed these disparate results.[47,48] When reviewing the clinical pain and experimental pain rating responses, no relationship between a subject's responsiveness to the thermal heat pulses and their current clinical pain was found. The present results are more consistent with those of Harkins et al.[49] who did not detect a relationship between how patients rated their thermal pain stimuli and their orofacial pain symptoms (i.e., jaw pain, jaw dysfunctions).[49]

Chronic orofacial pain in this patient sample resulted in a significant negative impact on functional ability and quality of life. Patients with moderate and severe pain were more psychologically distressed as indicated by lower scores on daily functional ability and quality of life measures. The observed findings of high severity scores from self-reported symptoms such as chemical sensitivity and quality of life are suggestive of a generalized negative affect which may be related to the negative bias or altered somatic perceptions in these TMJ implant patients. It is unclear whether these manifestations result from TMD or are causative factors. Multiple chemical sensitivity (MCS) is a recently recognized chronic disorder where patients report symptoms consistent with sensitivity to low level exposures to a number of common chemically unrelated

compounds.[52] Self- reported symptoms have been the sole basis for diagnosing MCS since no association with known biochemical agents has been established. Prevalence of MCS in the general population is unknown, and the estimate varies from 10%[53] to 33%.[54] Fibromyalgia patients often report a high frequency of non-musculoskeletal pain symptoms including those suggestive of MCS. A more recent report has shown that fibromyalgia patients with and without MCS do not differ in other symptomalogy. There have been no studies reported on the prevalence of chemical sensitivity in TMD patients. Thus, the chemical reactivity level represented in the present sample could be associated with the spectrum of conditions that includes fibromyalgia. However, the etiologic relationship between these disorders cannot be determined in this cross-sectional sample.

A high rate of comorbidity was observed between these TMJ implant patients and fibromyalgia, with 47% of the study sample and 80% in the severe pain group meeting the ACR criteria for fibromyalgia. High rates of comorbidity between myofascial pain and fibromyalgia have been suggested in several small clinical studies. Facial pain patients with myofascial pain diagnosis often reported widespread pain.[55-57] The study of Plesh et al found that 18.4% of TMD patients had fibromyalgia, and that 75% of these fibromyalgia patients satisfied criteria for myofascial TMD.[58] Our high reported rates far exceed the population prevalence rate of 2 percent for fibromyalgia.[59]

Based on physical examination, routine serology and other immunologic investigations, there was minimal evidence of an autoimmune disorder present or developing in these patients. Clinical evidence of systemic illness or autoimmune disease attributable to the implant material was not detected, similar to other reported findings.[38] One patient had limited features of SLE, but did not fully satisfy the criteria required for this diagnosis. However, the absence of autoantibodies

in this patient could reflect her ongoing treatment with methotrexate 10 mg once a week. Based on immune serology, this patient and three additional patients with residual Staphylococcus infections or prepatellar bursitis, did not have evidence of immunological abnormalities. When peripheral blood mononuclear cells were assessed for expression of cell surface antigens, which might be indicative of changes in immune status, the immune phenotypes of the cells in the TMJ implant patients were not significantly different from a group of healthy controls. No shift in lymphocyte subsets (CD4 or CD8), or in percent of B lymphocytes and natural killer cells was detected, consistent with the lack of significant evidence of clinical immune-based abnormalities. However, for TMJ implant patients with severe pain and fibromyalgia, changes in the percentages of T lymphocytes and of the CD8 T cell subset, in particular, may suggest involvement of, or impact on, the immune system. In a recent report, decreased serum levels of soluble CD8 were also noted in fibromyalgia patients and suggested to correlate with altered immune function.[60] While these data provide potential insight into an underlying immune modulation in association with fibromyalgia, further analyses is required to document such a relationship.

TMJ implants have been the subject of considerable public attention due to the well-documented complications following surgery. The exact number of implanted devices is unknown; it has been estimated to be as high as 20,000 implants.[61] The early positive clinical observations with Proplast/Teflon TMJ joint implants were followed by the long-term adverse outcomes. Despite efforts to remove the implants and their replacement with autogenous tissues, clinical response has been limited.

The variability for the symptom reports in different individuals with the same initial pathology remains unclear. Theories vary from peripheral sensitization where hyperalgesia may be involved as tenderpoints and thus contributes to induction of central

hyperexcitability,[62] to somatosensory amplification that results in heightening the experience of a particular disease.[63] Perhaps multiple mechanisms either alone or in combination give rise to these chronic pain disorders. Investigators have proposed that chronic fatigue syndrome, regional chronic pain syndromes, and emotional disorders are frequent comorbidities with fibromyalgia. Chronic fatigue syndrome and fibromyalgia involve central dysregulation of various axes of the stress response.[64-69] These studies have hypothesized that various forms of stress could mediate functional alterations in the hypothalamic-pituitary-adrenal axis, the sympathetic nervous system, other neuroendocrine axes, and serotonin metabolism,[70] which could constitute the basis for the diverse clinical manifestations in this spectrum of illness. Future studies elucidating the underlying mechanisms of the complex interactions between neuroendocrine hypofunction, the immune system, genetic susceptibility and pain may provide new approaches to the management of this chronic painful condition.

In conclusion, this group of TMJ implant patients demonstrated altered sensitivity to sensory stimuli, and diminished quality of life. There was little evidence to suggest autoimmunity in this patient population. Further studies with diseased and healthy controls may be beneficial to confirm the alterations in sensory sensitivity and to explore its mechanisms. Given the problems observed in this patient population, TMJ implant surgery for TMD should not be considered until new compelling evidence for the efficacy of implant surgery is obtained.

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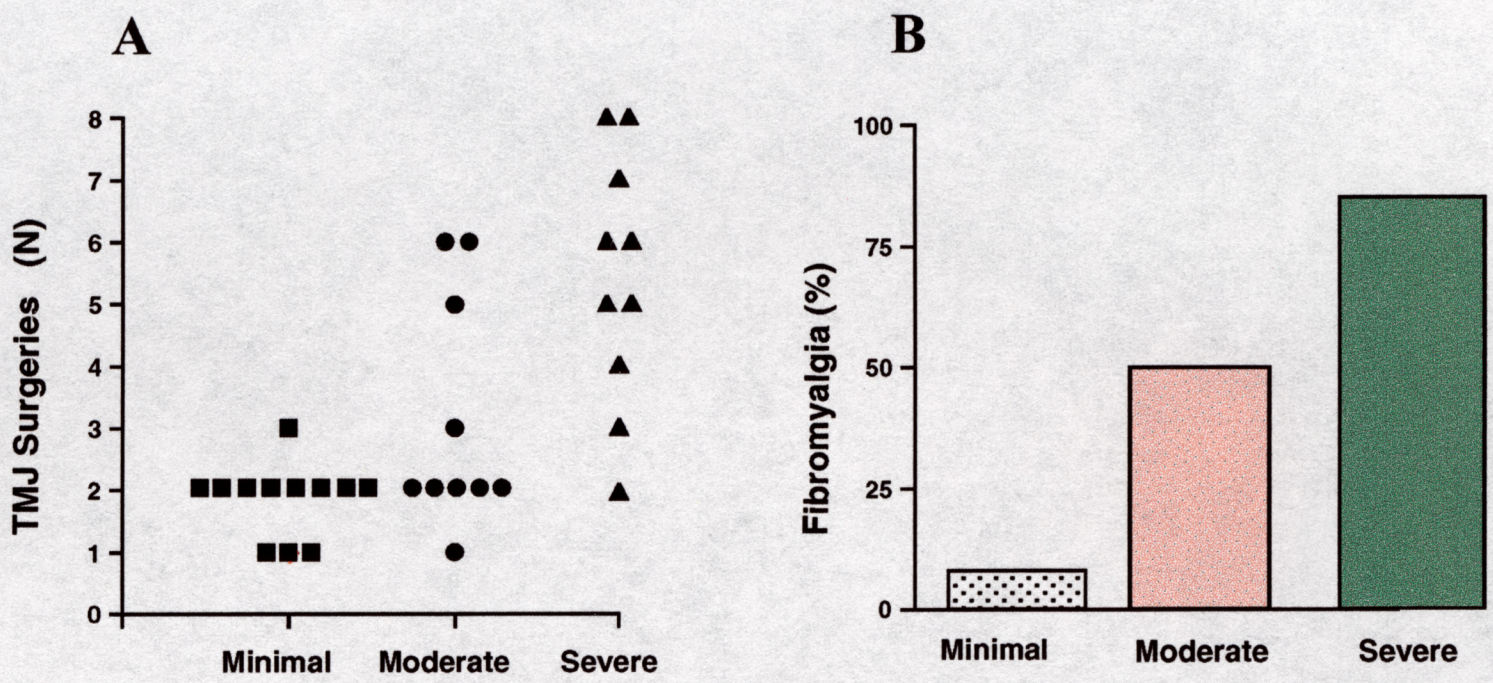
FIGURE 1



Overall Pain Intensity

FIGURE 2

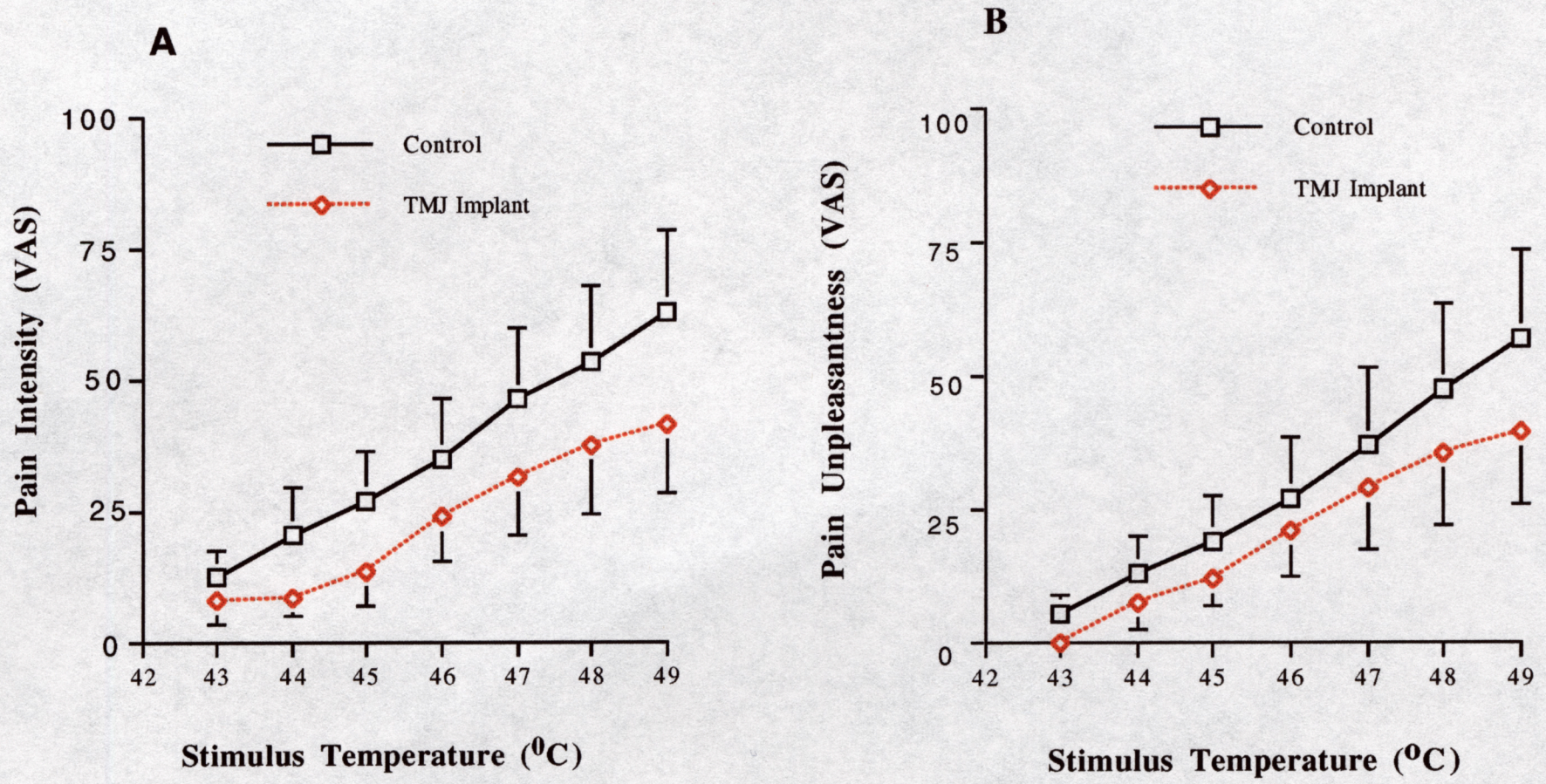

A
B
Pain Intensity (VAS)
Pain Unpleasantness (VAS)
100
75
50
25
0
Control
TMJ Implant
42
43
44
45
46
47
48
49
Stimulus Temperature (0C)
Stimulus Temperature (0C)

FIGURE 3

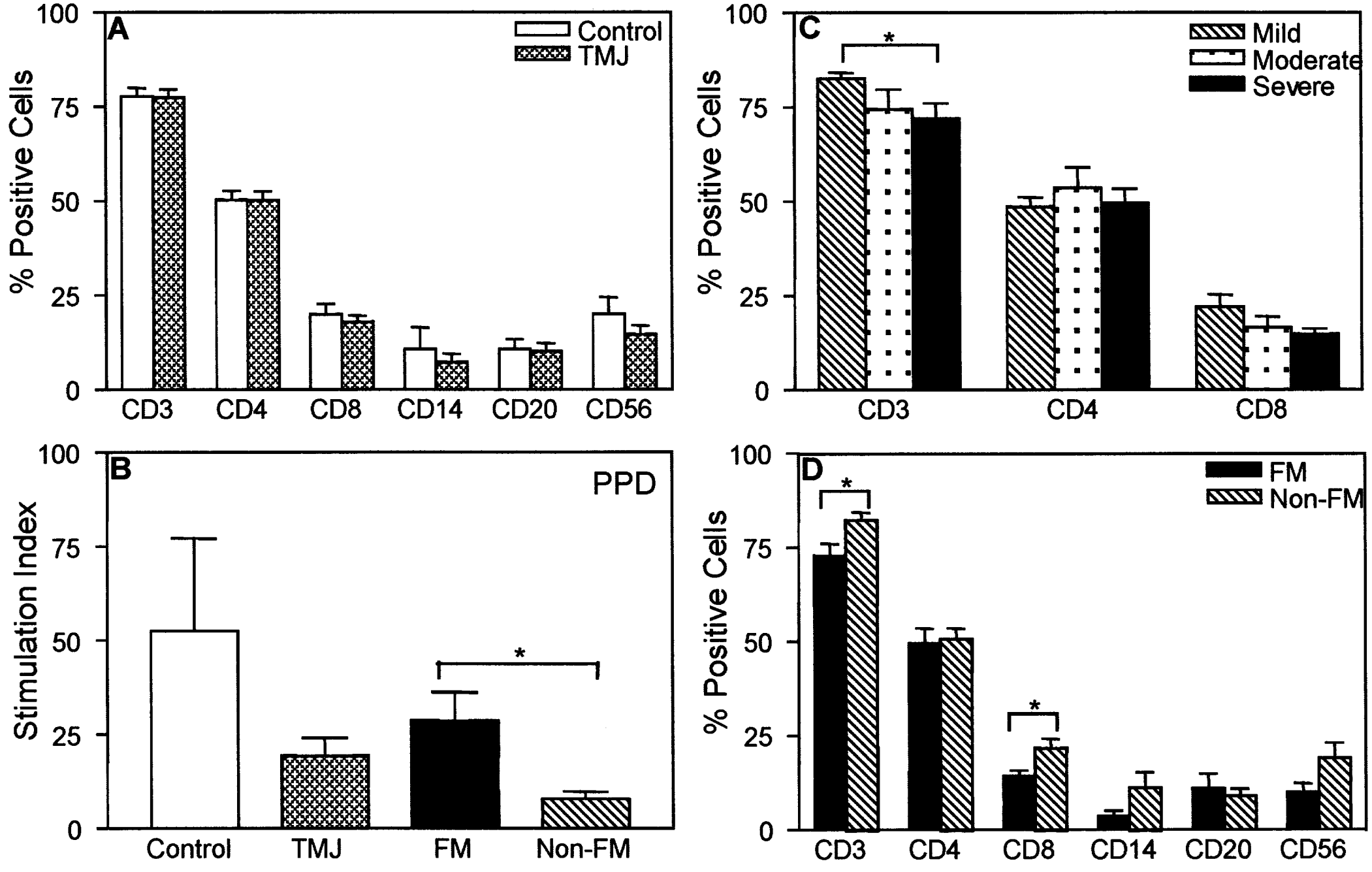

A
Control
TMJ
% Positive Cells
100
75
50
25
0
CD3
CD4
CD8
CD14
CD20
CD56
B
PPD
Stimulation Index
100
75
50
25
0
*
Control
TMJ
FM
Non-FM
C
Mild
Moderate
Severe
*
% Positive Cells
100
75
50
25
0
CD3
CD4
CD8
D
FM
Non-FM
*
*
% Positive Cells
100
75
50
25
0
CD3
CD4
CD8
CD14
CD20
CD56

Figure legends

Figure 1: Subjects were classified in three pain subgroups based on the VAS rating of their usual level of orofacial pain. The minimum pain (score ≤42), moderate pain (score >42 to<80) and severe pain (score ≥80 to100). The present pain intensity compared to number of TMJ surgeries are shown in the Panel (A). In Panel (B) present pain intensity compared to the percent of fibromyalgia diagnosis.

Figure 2: Mean values of pain VAS ratings in response to thermal stimulation are shown for TMJ implant patients and normal volunteer comparison group (errors bars indicate standard errors). Panel (A) shows ratings of Pain Intensity. Panel (B) shows ratings of Pain Unpleasantness.

Figure 3: Phenotypic analysis and proliferative responses of mononuclear cells from TMJ implant patients and healthy volunteer controls. Mononuclear cells were stained with antibodies to T cell (CD3, CD4, CD8), macrophage (CD14), B cell (CD20, and NK (CD56) surface antigens and analysed by FACS. The percentages of positive cells were compared between controls and TMJ implant patients (A), TMJ implant patients vs. pain responses (C), and TMJ implant patients with and without fibromyalgia (FM) (D). Mononuclear cells were stimulated with PPD (5 mcg/ml) and uptake of tritiated thymidine into DNA assessed (B). Stimulation index represents ratio of counts per minute in stimulated cultures to unstimulated cultures. N = 27 TMJ implant patients, 12 controls. *, P≤0.05

TABLE 1: PATIENT CHARACTERISTICS AND HISTORY OF SYMPTOMS

PATIENT CHARACTERISTICS (N=32)	
Age (years)	range = 36 –55 median = 47
Age of Onset	range = 13-35 median = 23
Gender	male = 5 female = 27
Joint Surgery (N)	total = 55 unilateral = 9 bilateral = 23
Duration of Implants (years)	range = <1-16 median = 10
Time since Removal (Years)	range = 1-16 median = 10
Number of Implants	in Place = 7 removed= 25

PRIOR TO IMPLANT SURGERY COMPLAINT (N=32)	
Jaw pain	10
Headache	5
Jaw locking	5
Jaw pain & clicking	4
Facial pain	3
Ear pain	1
Jaw clicking & locking	1
Headache & jaw clicking	1
Headache & jaw pain	1
Trauma	1

CURRENT CHIEF COMPLAINT (N=30)	
Jaw pain & mandibular dysfunction	22
Jaw pain	4
Mandibular dysfunction	2
Little to no pain	2

TABLE 2: OROFACIAL PAIN EVALUATION

TMD/RDC DIAGNOSES

TMJ arthralgia (III.A)	23
TMJ osteoarthritis (III.B)	21
Myofascial pain with limited opening (I.B)	21
TMJ osteoarthrosis (III.C)	8
Myofascial pain (I.A)	3

MANDIBULAR RANGE OF MOTION

Mn range (mm)	UO-NP	UO-P	AO-P
<10 - 16	3	2	2
17 - 33	14	13	12
34 – 50	10	12	13

UO-NP: unassisted opening without pain
UO-P: unassisted opening with pain
AO-P: assisted opening with pain

PAIN RESPONSES TO PALPATION TM AREA (%)

Location	None	Mild	Moderate	Severe
Temporalis	39	18	21	22
Masseter	48	7	22	23
Digastric	29	3	15	53
Submandibular Region	44	22	15	19
Lateral pterygoid	38	12	15	35
Tendon of Temporalis	30	12	23	35
Lateral pole (TMJ)	29	3	21	47
Posterior Attachment (TMJ)	38	12	12	38

Rating scores are none = 0, mild pain = 1, moderate pain = 2, and severe pain = 3.

TABLE 3: DISTRIBUTION BETWEEN LEVEL OF CLINICAL PAIN AT TIME OF EVALUATION AND OTHER FINDINGS

Orofacial Pain	Rheu[a]	Neurology[b]		PMR[c]	Psychiatry[d]		Psychology[e]	
Clinical Pain	FM	Headache		↓Cervical Range of Motion	Axis I (Mood Disorders)	Axis II (Personality Disorders)	Axis I (Mood Disorders)	Axis II (Personality Disorders)
		Tension	Migraine					
Minimal Pain	8%	0%	17%	16%	42%	14%	73%	64%
Moderate Pain	40%	30%	30%	20%	40%	0%	90%	80%
Severe Pain	80%	20%	10%	60%	50%	33%	90%	70%

Abbreviation: FM: fibromyalgia, Rheu: Rheumatology, PMR: Physical medicine and rehabilitation.
The number of patients evaluated for each discipline are listed below.
[a]Rheumatology, n=31
[b]Neurology, n=23
[c]Physical medicine and rehabilitation, n=23
[d]Psychiatry, n=18
[e]Psychology, n=29

TABLE 4: PERCENT OF TMJ IMPLANT PATIENTS WITH HIGH QUEESI SCORES

		CLINICAL PAIN *POST-HOC* CLASSIFICATION		
	HIGH CRITERIA[φ]	MINIMAL	MODERATE	SEVERE
Symptom Severity (n=29)	≥ 40	18% (2/11)	60% (6/10)	88% (7/8)
Chemical Intolerances (n=29)	≥ 40	36% (4/11)	50% (5/10)	63% (5/8)
Other Intolerances (n=29)	≥ 25	9% (1/11)	60% (6/10)	88% (7/8)
Impact on Life (n=27)	≥ 24	20 % (2/10)	40% (4/10)	71% (5/7)

The self-reported QUEESI consists of the four core scales of symptom severity, chemical intolerances, other intolerances and impact on life. Abnormal values consist of those exceed the high criteria.
[φ]The high criteria cut off are the values set by Miller and Prihoda, 1999.

TABLE 5: PERCENT OF TMJ IMPLANT PATIENTS WITH LOWER SF-36 SCORES

	NORMAL POPULATION (N=504)	CLINICAL PAIN *POST-HOC* CLASSIFICATION		
	Ware 1997	MINIMAL	MODERATE	SEVERE
Physical Functioning (n=31)	89.70 ± 16.35	17% (2/12)	40% (4/10)	100% (9/9)
Social Functioning (n=29)	85. 75 ± 21.04	8% (1/12)	20% (2/10)	86% (6/7)
Role Limitations (physical) (n=31)	86. 66 ± 28.92	17% (2/12)	70% (7/10)	100% (9/9)
Role Limitations (emotional) (n=30)	82.76 ± 31.26	0% (0/12)	22% (2/9)	44% (4/9)
Body Pain (n=31)	77.06 ± 22.11	17% (2/12)	40% (4/10)	79% (7/9)
Mental Health (n= 31)	75.12 ± 16.69	0% (0/12)	0% (0/10)	11% (1/9)
Vitality (n= 31)	62.42 ± 19.43	8% (1/12)	40% (4/10)	33% (3/9)
General Health Perception (n=29)	75.87 ± 17.86	17% (2/12)	40 % (4/10)	57 % (4/7)

The 36-item Short Form Health Survey (SF-36) is a general health status instrument, it includes bodily pain and physical function scales as well as scales that evaluate social, mental, and emotional construct. Subjects have scores below and outside of normal range are listed for each health domain.